REMARKS

Formal Matters

Claims 43, 46, 47, 51 and 54, as well as newly added Claims 55 to 58, are pending after entry of the amendments set forth herein.

Amendments

The Applicants have amended Claims 43 and 51 to limit the condition being treated to epilpepsy. Support for this amendment is found in previously pending claims 45 and 53. Newly added Claims 55 to 62 find support in the specification at page 6, line 26 to page 7, line 4. As the above new claims introduce no new matter to the application, their entry by the Examiner is respectfully requested.

It is noted that the above amendments to the claims limiting the condition to epilepsy have been made solely in order to expedite prosecution of the present application to allowance, and in no way should be viewed as an acquiescence by the Applicant to the Examiner's position that the original scope of the claims is not fully patentable. The Applicants expressly reserve the right the pursue claims of the original scope in one or more subsequent applications.

Rejections

35 U.S.C. § 112, 1st ¶

The specification was objected to, and Claims 43-44, 46-52 and 54 were correspondingly rejected, under 35 U.S.C. § 112, 1st ¶. In view of incorporation of the limitations of Claims 45 and 53 into Claims 43 and 51, this rejection may be withdrawn.

35 U.S.C. § 103

Claims 43-54 were rejected under 35 U.S.C. § 103 as being unpatentable over Freidrich, Okajima, Veronesi and Pinsky, in view of Kazmirowski. In making this

rejection, the Examiner reasoned that the cited primary references teach the general approach of treating neurological conditions with protease inhibitors, and the supplemental Kazmirowski reference discloses the specific aminobenzenesulfonyl compounds employed in the experimental section. As such, the Examiner reasons that what the applicants have done is merely elucidate the mechanism of a method that has been inherently practiced in the prior art, and therefore have not made a patentable invention.

With respect to the pending claims as amended above, these claims are directed to the treatment/prevention of epilepsy. It is respectfully submitted that, absent the data provided in the present application and working exemplification, one of skill in the art would not have found it obvious to employ serine protease inhibitors for the treatment of epilepsy as specified in the claims because the cited prior art references provide no suggestion or guidance as to the effectiveness of serine protease inhibitors in the treatment of epilepsy.

Claims 43-54 are specifically directed to treating epilepsy. The Applicants have made these claims following their observed results of the Kindling Assays reported in the experimental section of the present application. The Kindling Assay employed by the Applicants is well accepted by those of skill in the art as a model of human conditions that result from undesirable synaptic responsiveness, e.g. epilepsy. As such, the Kindling Assay employed by the Applicants is an art accepted model of human epilepsy and related disease conditions associated with increased synaptic drive and/or responsiveness. In fact, the Kindling Assay is the major art accepted model of epilepsy, and any other type of assay is generally not accepted as indicative of what will, and will not be, effective in treating epilepsy and related disorders. See e.g., McNamara JO, Psychiatry Clin Neurosci. (1995) 49(3):S175-8; McNamara et al., CRC Crit Rev Clin Neurobiol. (1985) 1(4):341-91; and Sutula TP, Epilepsia. (1990) 31 Suppl 3:S45-54.

In the work performed by the Applicants, the Applicants showed that serine protease inhibitors were effective in treating symptoms brought about in the Kindling

Assays. As such, only after the Applicants showed that serine protease inhibitors are effective in the Kindling Assay would one of skill in the art have a reasonable expectation of success that serine protease inhibitors would exhibit any activity, much less desirable therapeutic activity, in treating epilepsy.

Turning now to the cited references, Freidrich provides experimental evidence directed to the use of antithrombin compounds to promote neurite growth. Showing that an agent increases neurite growth teaches nothing about whether it is useful in the treatment of epilepsy. As such, one of skill in the art would have no idea based on Freidrich as to whether serine protease inhibitors would have any effect, much less a therapeutic effect, on epilepsy, as is now claimed. As pointed out above, one of skill in the art can not know whether a particular type of agent will have activity therapeutic activity with respect to epilepsy unless a representative of that particular type of agent is tested in a Kindling Assay.

Okajima describes the use of antithrombin III for prevention and treatment of "motor functional disturbance, tissue injury, spinal injury, and spinal ischemia." Since Okajima reports no Kindling Assay data and does not even mention the particular disease conditions that are the subject of the presently pending claims after entry of the above amendment, Okajima also fails to provide any indication that serine protease inhibitors will have any activity, much less a therapeutic activity, with respect to the treatment of epilepsy as now claimed.

Veronesi reports using PMSF to protect rats from neurological damage following exposure to Mipafox. As such, this report is based on preventing damage following exposure to a neurotoxin. Since Veronesi is concerned with preventing the effects of a neurotoxin, Veronesi says nothing about the disease conditions that are the subject of the pending claims. Since Veronesi reports no Kindling Assay data and does not even mention the particular disease conditions that are the subject of the presently pending claims after entry of the above amendment, this reference also fails to provide any

indication that serine protease inhibitors will have any activity, much less a therapeutic activity, with respect to the treatment of epilepsy as now claimed.

Pinsky reports the effect of peptidase inhibitors on rats undergoing narcotic withdrawal. Since Pinsky is concerned with the effects of narcotic withdrawal, Pinsky says nothing about the disease conditions that are the subject of the pending claims. While Pinsky calls the symptoms "eleptiform," this merely describes the seizures, not the condition being treated, which is narcotic withdrawal. Since Pinsky reports no Kindling Assay data, this reference also fails to provide any indication that serine protease inhibitors will have any activity, much less a therapeutic activity, with respect to the treatment of epilepsy as now claimed.

As such, the primary references, i.e., Freidrich, Okajima, Veronesi and Pinsky, all fail to provide any guidance as to the activity of serine protease inhibitors with respect to treatment of disease conditions that are the subject of the presently pending claims following entry of the above amendment.

As Kazmirowski has been cited solely for the teaching of a specific class of compounds as serine protease inhibitors, Kazmirowski fails to make up the fundamental deficiencies in the primary references.

Accordingly, the presently pending as amended above are not obvious over the combined teaching of Freidrich, Okajima, Veronesi and Pinsky, in view of Kazmirowski and are therefore patentable over the combined teaching of these references.

Conclusion

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number THUR001.

Respectfully submitted,
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Date: September 23, 2003

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